HIV INFECTION: FROM PATHOGENESIS TO NEW TREATMENT OPTIONS
Milano, 2 Maggio 2024
Centro Congressi StarHotels Ritz

HTE: nuove opzioni terapeutiche

Antonella Castagna

Financial Disclosures

Gilead Sciences, ViiV Healthcare, Janssen-Cilag, MSD, Menarini, Angelini, Pfizer

Salvage Therapy Including Foscarnet and Ibalizumab for Multidrug-Resistant HIV 2 Infection

Patient Number	CDC Stage	CD4 (/mm^3)	Viral Load (log10 Copies/mL)	Cumulative Genotyping Results: Reverse transcriptase	Protease	Integrase	Genotypic Susceptibility Score	Last Regimen	Multiple ARV Therapy +/– PFA Induction	Time of Viral Suppression
	A	80	3	K65R N69S Y115F M184V S215Y	I54M I84V L90M	N155H E92Q T97A	0	DRV/r (800/100 mg QD) FTC/TDF (200/245 mg QD) MVC (150 mg BID)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (1000/100 mg BID) ZDV (250 mg BID)	Not achieved at W24
	C	25	4.6	K65R N69S	I50V	E92Q T97A	3	SQV/r (500/100 BID) FTC/TDF (200/245 mg QD)	ZDV/3TC (300/150 mg BID) DTG (50 mg BID) ATV (150 mg QD) LPV/r (400/100 mg BID)	Not achieved at W24
	A	86	4.3	K65R M184V	V47A	E92Q T97A N155H	2	FTC/TDF (200/245 mg QD) RAL (400 mg BID)	ZDV/3TC (300/150 mg BID) DTG (50 mg BID) ATV (150 mg QD) DRV/r (600/100 mg BID) + PFA induction	Day 0 IBA
	C	70	4	K65R N69S M184V	I54M I84V L90M	G140A Q148K	2	FTC/TDF (200/245 mg QD) DRV/r (800/100 mg BID)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (600/100 mg BID) ZDV (250 mg BID) + PFA induction	Not achieved at W24
	C	160	3.6	K65R Y115F M184V	V47A I84V	E92Q T97A G140S Y143C/G Q148R	1.5	DRV/r (600/100 mg BID) DTG (50 mg BID)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (600/100 mg BID) ZDV (250 mg BID) + PFA induction	Not achieved at W24
	C	20	4	K65R K70R V111I Q151M M184V	I54M I82F L90M	E92Q T97A N155H	0	3TC (300 mg QD) DRV/r (800/100 mg BID)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (800/100 mg BID) ZDV (250 mg BID) + PFA induction	Not achieved at W24
	B	360	3.1	K70N V111I M184V S215F	I50V I54M I84V L90M	E92Q T97A Y143R N155H	1	ABC/3TC (600/300 mg QD) DRV/r (800/100 mg QD) TDF (245 mg) DTG (50 mg QD) ATV (150 mg QD)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (600/100 mg BID)	W4 IBA
	A	170	2.4	K65R D67N V111I M184V	V47A I50V	T97A Y143G/C	1.5	MVC (150 mg BID) DRV/r (600/100 mg BID) DTG (50 mg BID) ZDV (250 mg BID) ATV (150 mg QD)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (600/100 mg BID) ZDV (250 mg BID) + PFA induction	Day 0 IBA
	C	46	2.8	M184V	I50V I54M	No mutation	3	FTC/TDF (200/245 mg QD) DRV/r (800/100 mg BID) DTG (50 mg BID) ATV (300 mg) MVC (150 mg BID)	BIC/FTC/TAF (50/200/ 25 mg QD) DTG (50 mg QD) ATV (150 mg QD) DRV/r (600/100 mg BID) ZDV (250 mg BID) + PFA induction	Not achieved at W24

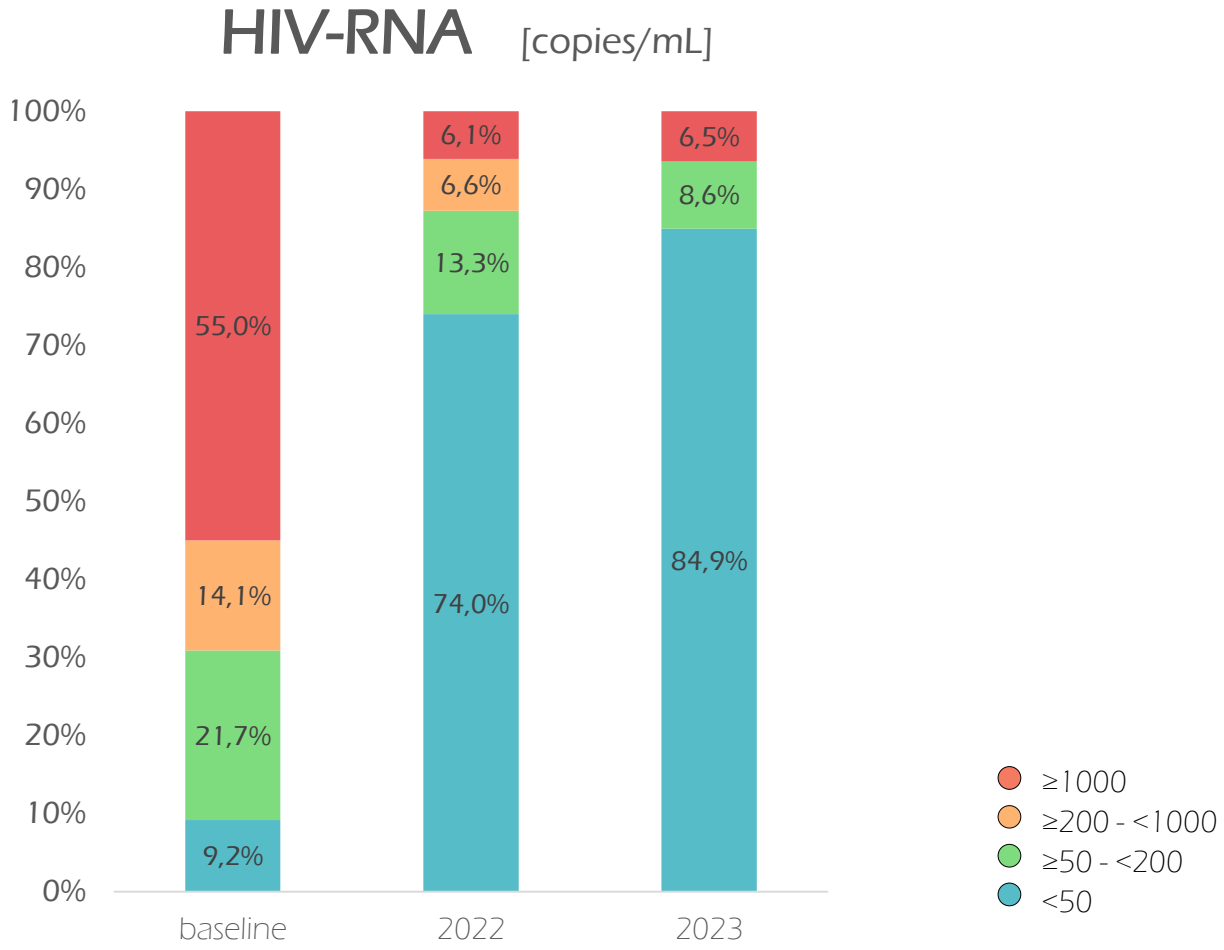
A.Bachelard, CID 2024

Antiretroviral drugs in PWH enrolled in PRESTIGIO

		2021 (n=205)	2022 (n=206)	2023 (n=205)
Drugs	DTG	159 (77,6%)	154 (74,8%)	153 (74,6%)
	DRV/r	87 (42,4%)	74 (35,9%)	74 (36,1%)
	DRV/c	55 (26,8%)	61 (29,6%)	58 (28,3%)
	XTC	102 (49,8%)	108 (52,4%)	110 (53,7%)
	TAF	74 (36,1%)	79 (38,3%)	83 (40,5%)
	TDF	15 (7,3%)	15 (7,3%)	12 (5,9%)
	DOR	27 (13,2%)	32 (15,5%)	36 (17,6%)
	ETV	29 (14,1%)	24 (11,7%)	20 (9,8%)
	RPV	12 (5,9%)	11 (5,3%)	10 (4,9%)
	MVC	40 (19,5%)	43 (20,9%)	41 (20,0%)
	FTR	11 (5,4%)	24 (11,7%)	34 (16,6%)
	LEN	8 (3,9%)	8 (3,9%)	9 (5,3%)
	IBA	5 (2,4%)	8 (3,9%)	5 (2,5%)
	ISL	3 (1,5%)	3 (1,5%)	3 (1,5%)
	ENF	2 (1,0%)	4 (1,9%)	2 (1,0%)

Data updated to March 1st, 2024

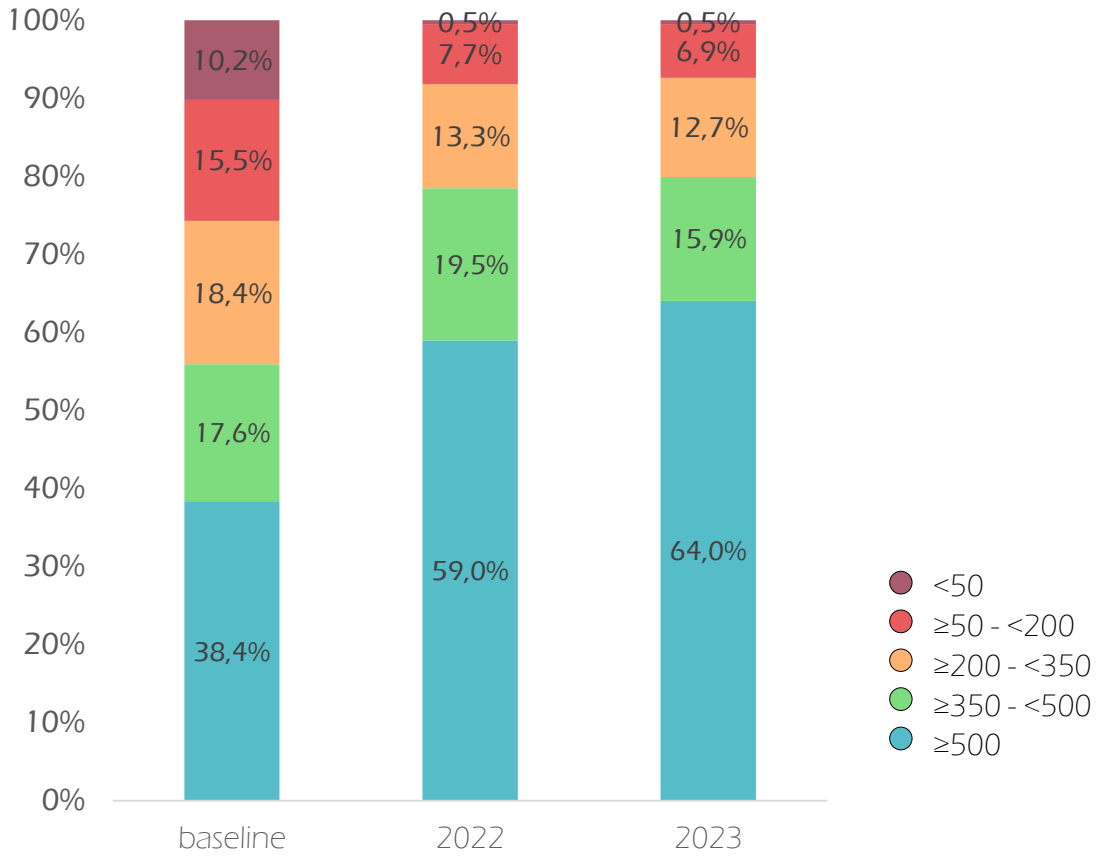
PRESTIGIO REGISTRY UPDATE



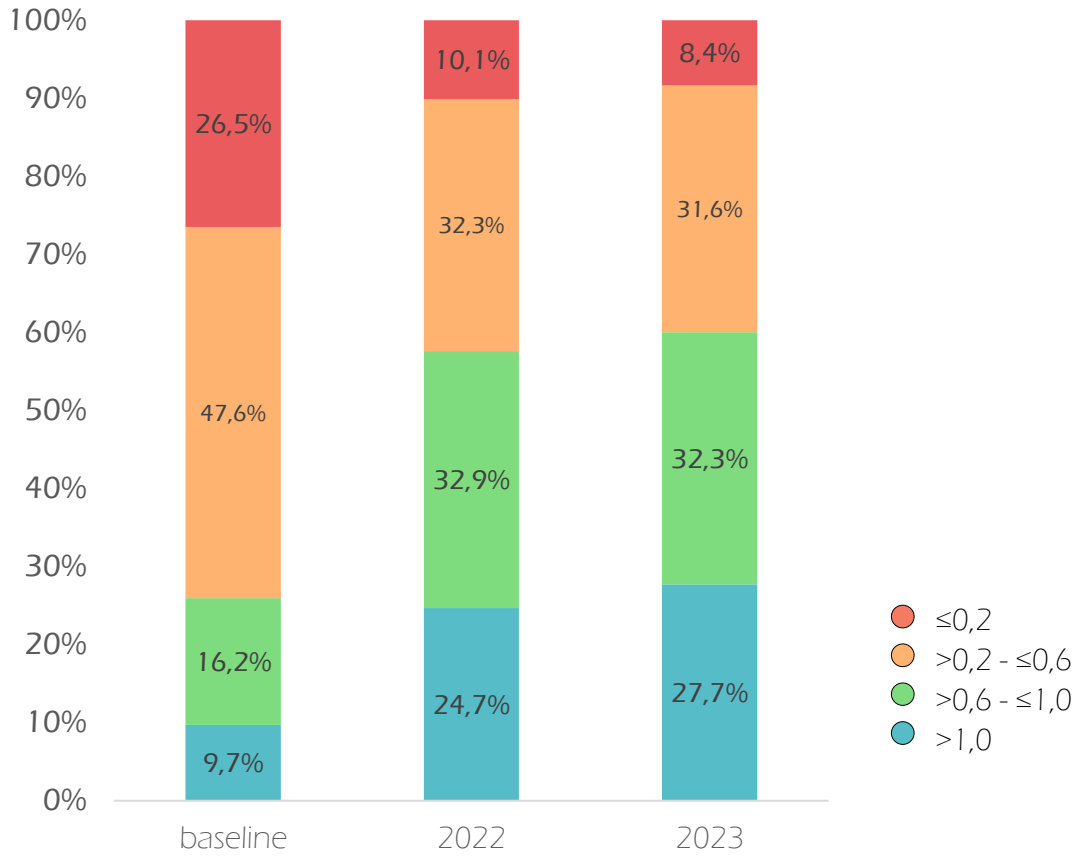
Data updated to March 1st, 2024

PRESTIGIO REGISTRY UPDATE

CD4+ [cells/µL]



CD4/CD8 [ratio]



PRESTIGIO Registry meetING on HIV multidrug resistance

Data updated to March 1st, 2024

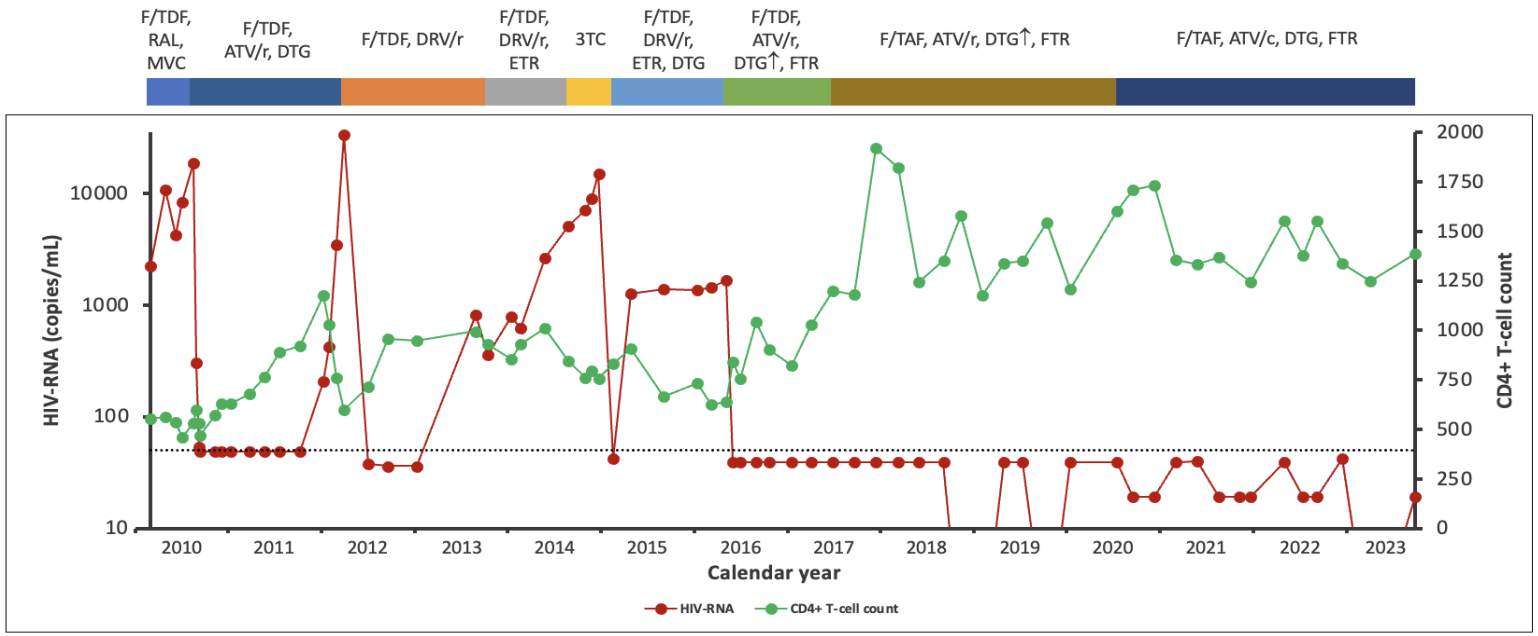
CLINICAL EVENTS IN PWH ENROLLED in PRESTIGIO

	HIV-related	
	until 2022	until 2023
C events	26	27
AIDS-defining malignancies	7	8
B events	36	39
	69	**74**

	non HIV-related	
	until 2022	until 2023
Non HIV-related infectious events	90	100
Neuropsychiatric diseases	47	51
Musculoskeletal diseases	29	30
CKD	32	32
Cardiovascular disorders	36	41
Non-AIDS-defining malignancies	27	30
anal carcinoma	7	8
Hodgkin's lymphoma	4	4
epatocellular carcinoma	2	2
bladder cancer	2	2
lung cancer	1	1
other malignancies	11	13
Urinary tract diseases	15	17
Liver events	14	16
Diabetes	12	13
COPD	6	6
	308	**336**

Data updated to March 1st, 2024

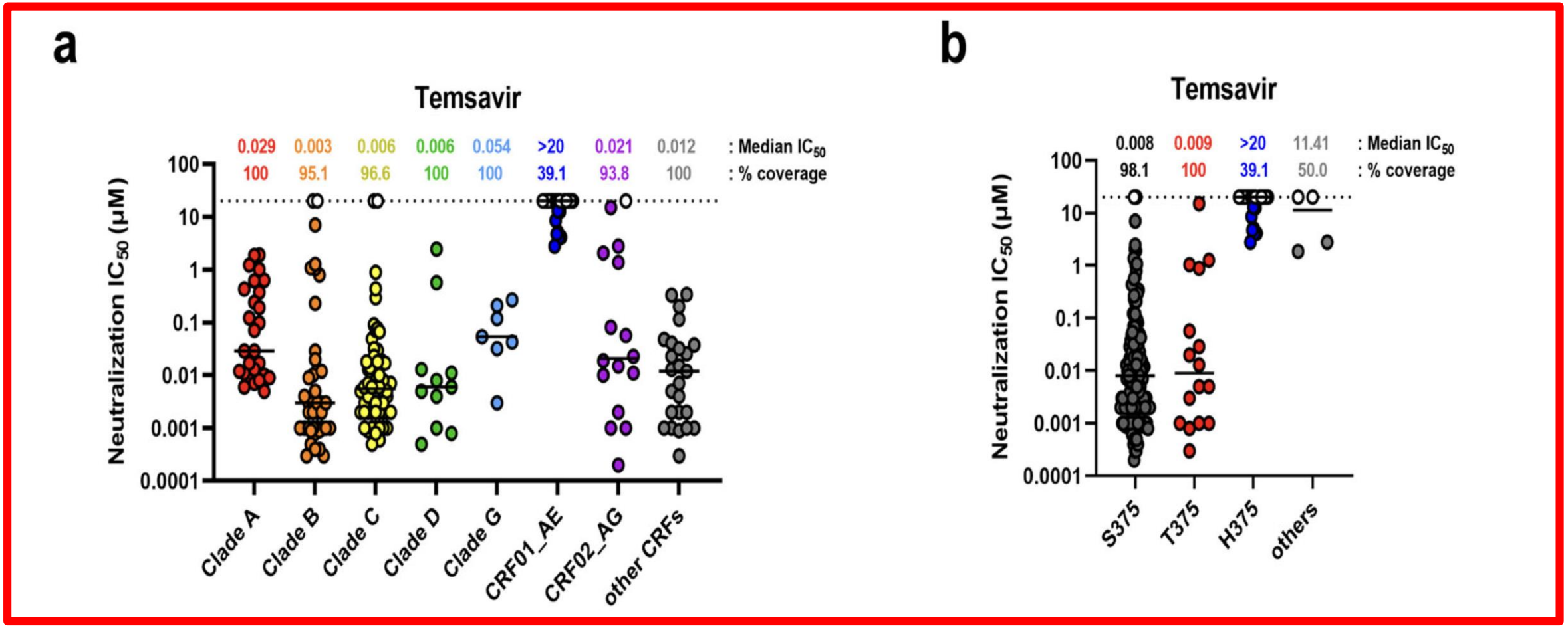
Long-term outcome in a person with pandrug-resistant HIV: the added value of a multidisciplinary approach



	NRTIs	NNRTIs	PIs	INSTIs
Major resistance mutations on cumulative RNA-based genotype at FTR start	M41L, A62V, D67N, V75I, M184IV, L210W, T215EY, K219ER	K103N, E138G, Y188L, H221Y, K238T	V32I, M46I, I47V, I50V, I54L, L90M	E138K, G140S, Q148H
Active ARVs according to cumulative RNA-based genotype at FTR start	-	-	-	-
Active ARVs according to phenotype at FTR start	-	-	ATV/r, IDV/r, TPV/r	-

T Clemente, JAC-Antimicr Resist

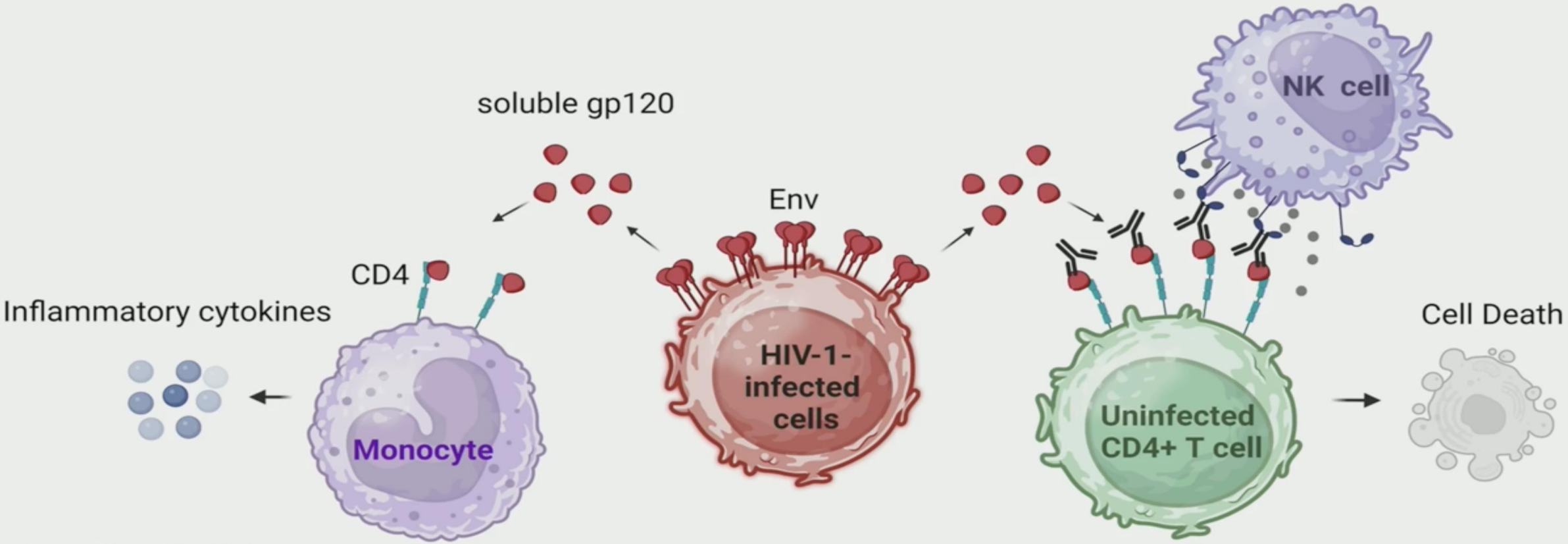
Structure-function analyses reveal key molecular determinants of HIV-1 CRF01_AE resistance to the entry inhibitor temsavir



J Prevost, Nat Commun

Soluble gp120 is immunomodulatory *in vitro*

1. **Induces the release of proinflammatory cytokines**
2. **Sensitizes uninfected bystander cells to ADCC**



CRCHUM CENTRE DE RECHERCHE

Richard et al., 2016; Richard et al., 2018, Richard et al., 2023

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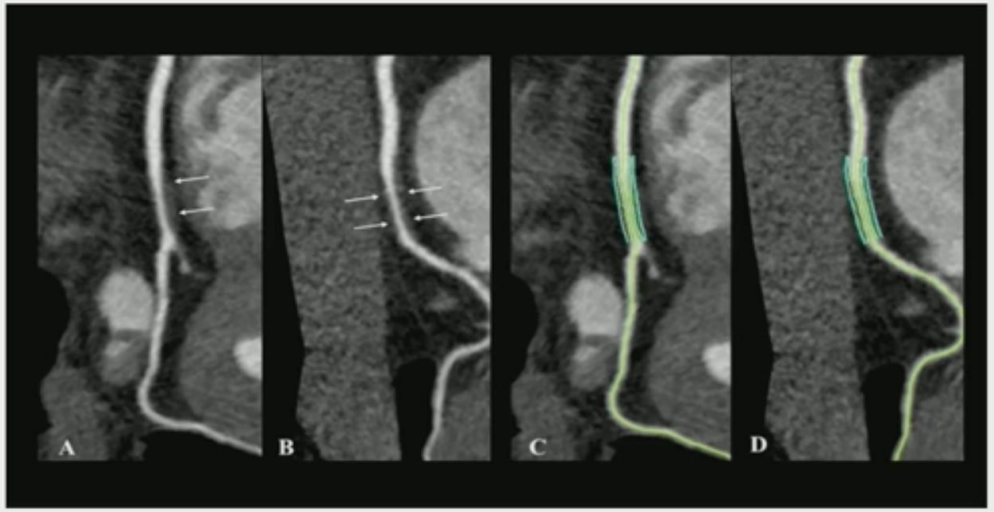
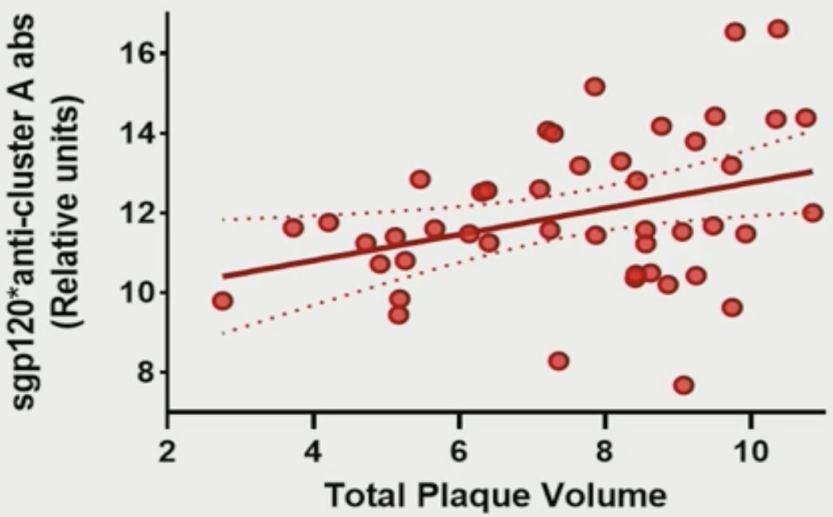
M Benlarbi, CROI 2024

sgp120 and anti-cluster A antibodies are associated with volume of atherosclerotic plaques on CT

Computed Tomography Coronary Angiography (CTCA)





Crude association

Beta (95% CI)	*P value*
0.36 (0.06 to 0.66)	**0.03**

Adjusted association

Beta (95% CI)	*P value*
0.41 (0.13 to 0.69)	**0.006**

BMC Infect Dis 2017 Vol. 17 Issue 1 Pages 611
Radiology 2021 Jun;299(3):571-580

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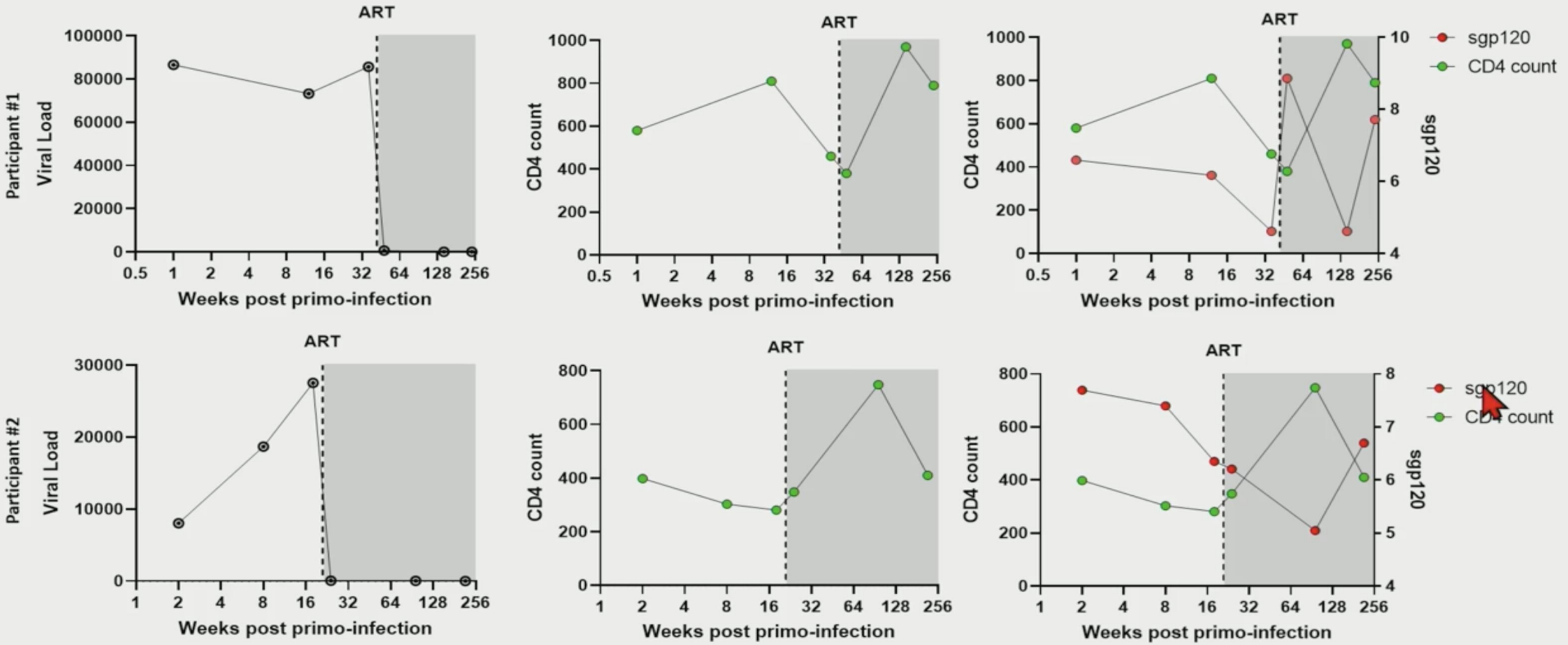
Longitudinal evaluation of sgp120



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M Benlarbi, CROI 2024

RECRUITING

Changes in Immunologic Parameters Following the Addition of Fostemsavir in Virologically Suppressed Immunologic Non-responders Living With HIV-the RECOVER Study

ClinicalTrials.gov ID NCT05220358

Sponsor Orlando Immunology Center

Information provided by Orlando Immunology Center (Responsible Party)

Last Update Posted 2023-11-03

J Antimicrob Chemother
https://doi.org/10.1093/jac/dkae121

Fostemsavir to overcome drug–drug interactions in heavily treatment-experienced people with HIV and cancer

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Case Report

Lenacapavir with Fostemsavir in a Multidrug-Resistant HIV-Infected Hemodialysis Patient

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Lenacapavir Efficacy in CAPELLA Patients with No Fully Active Agents in Optimized Background Regimen

Table 1. Participants' Baseline OBRs and ARV Activity Profiles

Participant	OBR		OBR OSS	Activity of antiretrovirals at baseline																				
				INSTIs				NNRTIs				NRTIs						PIs					EIs			
	No activity	Partial activity		BIC	DTG	EVG	RAL	DOR	EFV	ETR	RPV	3TC	FTC	ABC	ddI	TFV*	ZDV	FPV	ATV	DRV	LPV	TPV	FTR	MVC	ENF	IBA
1	3TC, DRV/c, DTG, ENF, MVC	-	0																							
2	FTC, DOR, BIC, IBA	TAF	0.5																							
3	3TC, RPV, MVC, IBA	-	0																							
4	FTC, DRV/r, DTG, IBA	TAF	0.5																							
5	FTC, TDF, DRV/r, DTG	-	0																							
6	FTC, DRV/r, DTG, IBA, FTR	TAF	0.5																							
7	FTC, DOR, DRV/c	TAF	0.5																							
8	DOR, DTG	-	0																							
9	FTC	TAF, DRV/c	1																							
10	DOR, IBA, FTR	-	0																							
11	DRV/r, DTG	TDF	0.5																							
12	DOR	DTG	0.5																							

No activity Partial activity Full activity No data

Per FDA Snapshot algorithm, 10/12 participants had HIV-1 RNA <50 copies/mL at ≥1 of the three predefined visits (Week 26, Week 52, or Week 104), and 8/12 participants were suppressed at all three visits

ISL and LEN Collaboration

HIV treatment regimens with high efficacy, favorable tolerability and DDI profile, extended dosing and various modes of administration are required to address current unmet needs, daily dosing/injection fatigue, help avoid HIV-related stigma and simplify accessibility

Merck and Gilead partnered to co-develop* LAO (QW) and LAI combinations of investigational ISL and LEN for HIV treatment[1]

ISL is a NRTTI with multiple mechanisms of action

LEN is a first-in-class capsid inhibitor that inhibits HIV replication at multiple points in the viral lifecycle

Both compounds exhibit long half-lives that allow for lower dosing frequency (i.e. QW and LAI)

No DDI between ISL and LEN[2]

ISL and LEN have potent antiretroviral activity at low doses

ISL and LEN have an additive inhibition of HIV-1 replication; no antagonism or cross-resistance observed between ISL and LEN[3]

*Collaboration will include co-development and co-commercialization globally
DDI, drug-drug interaction; ISL, islatravir; LAO, long-acting oral; QW, weekly
1. Gilead Sciences and Merck. Press Release 15 Mar 2021; 2. Zhang H, et al. CROI 2022. Poster 433; 3. Diamond T, et al. CROI 2023, Poster 585

‡

ISL + LEN LAO in VS PLWH

Phase 2, randomized, open-label, active-controlled, multicenter study to evaluate safety, efficacy and PK of ISL + LEN in VS PLWH (N=100)‡

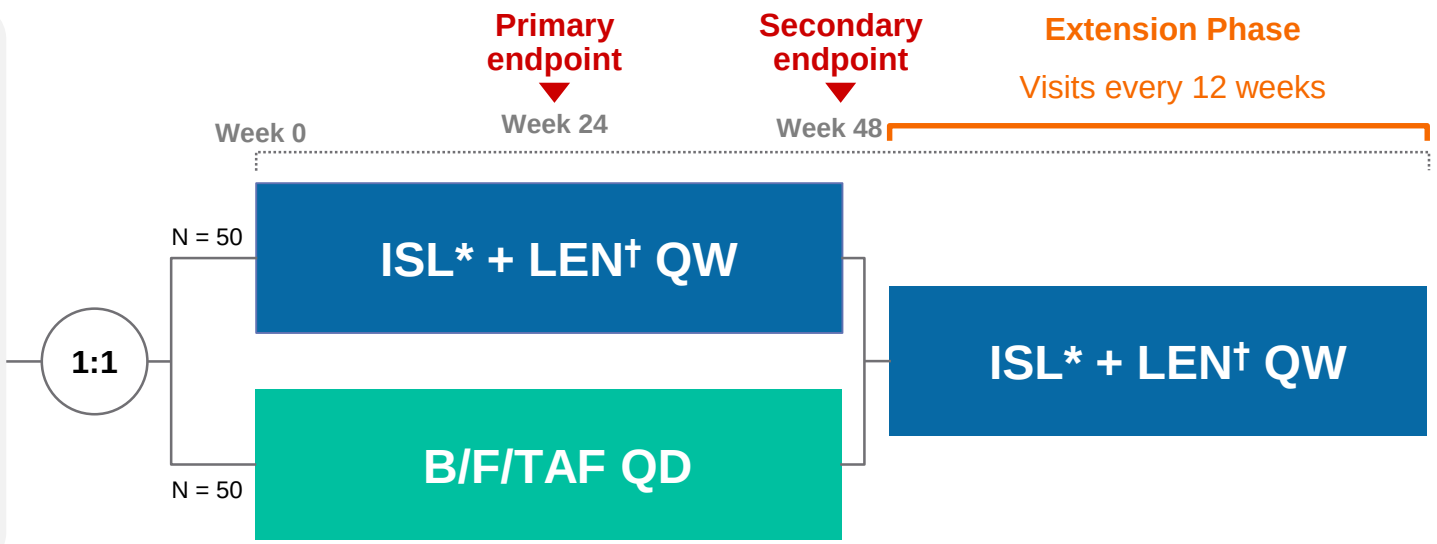
VS PLWH

≥18 years old

On B/F/TAF for ≥ 24 weeks

HIV-1 RNA < 50 c/mL for ≥ 24 weeks

CD4+ T-Cells ≥ 350 cells/mm^3



Primary endpoint

% with HIV-1 RNA ≥ 50 c/mL at Week 24

Secondary endpoints

- % with HIV-1 RNA ≥ 50 c/mL and < 50 c/mL at Weeks 12, 24 and 48
- Change in CD4+ cell count at Weeks 12, 24, and 48
- Safety, tolerability, PK and PROs§

*ISL dosing: **Day 1:** 2 mg [2 × 1 mg capsule]; **Day 8 and QW thereafter:** 2 mg [2 x 1 mg capsule]
†LEN dosing: **Day 1:** 600 mg [2 × 300 mg tablets]; **Day 2:** 600 mg [2 × 300 mg tablets]; **Day 8 and every week thereafter:** 300 mg [1 x 300 mg tablet]

ISL, islatravir; LAO, long-acting oral; PK, pharmacokinetics; PROs, patient reported outcomes; QW, weekly; VS, virologically suppressed
‡Study design, inclusion criteria, and endpoints depicted for Cohort 2
§ PROs are exploratory endpoints

ClinicalTrials.gov identifier: NCT05052996. Updated Dec 21, 2022. Accessed January 6, 2023. https://clinicaltrials.gov/ct2/show/NCT05052996. Data on file.

Phase II Trial of Oral Weekly ISL + LEN: Baseline Demographics

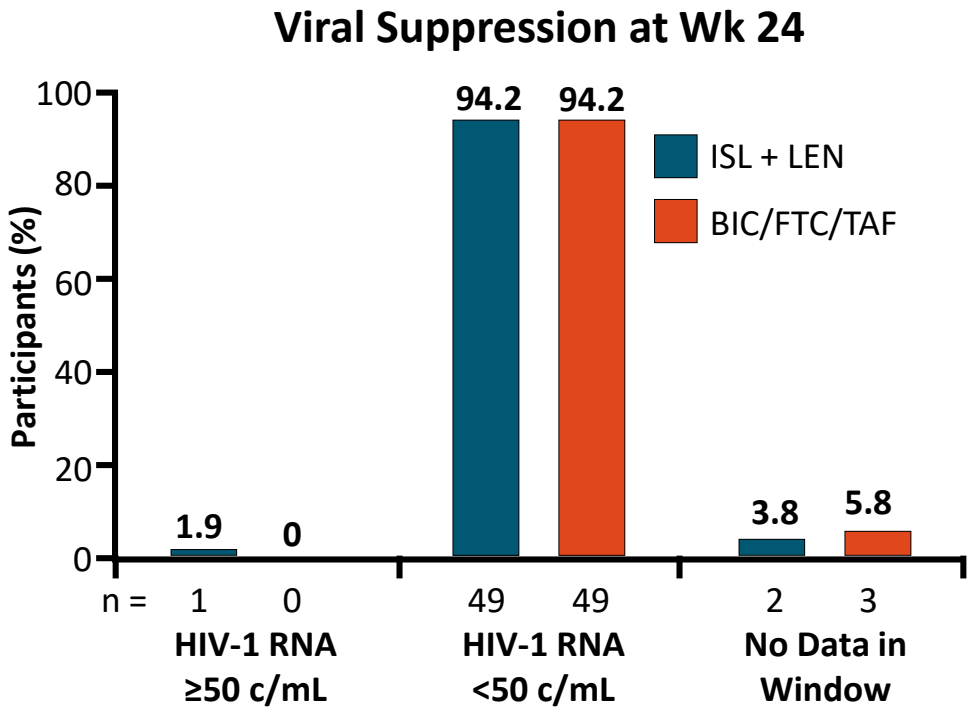
Characteristic, n (%)	Total (N = 104)	ISL + LEN (n = 52)	BIC/FTC/TAF (n = 52)
Median age, yr (range)	40 (26-76)	40 (28-67)	40 (26-76)
Female at birth	19 (18.3)	10 (19.2)	9 (17.3)
Gender identity			
▪ Transgender	1 (1.0)	1 (1.9)	0
▪ Nonbinary/third gender	1 (1.0)	0	1 (1.9)
Race			
▪ White	52 (50.0)	25 (48.1)	27 (51.9)
▪ Black	37 (35.6)	21 (40.4)	16 (30.8)
▪ Asian	3 (2.9)	2 (3.8)	1 (1.9)
▪ American Indian or Alaska Native	3 (2.9)	1 (1.9)	2 (3.8)
▪ Native Hawaiian or Pacific Islander	1 (1.0)	0	1 (1.9)
▪ Other	8 (7.7)	3 (5.8)	5 (9.6)
Ethnicity, Hispanic or Latino/a	30 (28.8)	13 (25.0)	17 (32.7)
Mean (SD) CD4, cells/mm^3, mean (SD)	786 (249.5)	755 (223.6)	818 (271.3)
▪ ≥500 cells/mm^3	96 (92.3)	46 (88.5)	50 (96.2)
Mean (SD) ALC x 10^3/μL, mean (SD)	1.94 (0.556)	1.94 (0.445)	1.95 (0.652)

Colson. CROI 2024. Abstr 208.

Slide credit: clinicaloptions.com

Phase II Trial of Oral Weekly ISL + LEN: Efficacy at Wk 24

- High rates of virologic suppression maintained in both treatment arms



- Individual receiving ISL + LEN with HIV-1 RNA ≥50 c/mL at Wk 24 resuppressed at Wk 30 without treatment change
  - Adequate drug levels per PK
  - Emergent resistance not detected

Visit	HIV-1 RNA, c/mL
Screening	<50
Day 1	251
Wk 24	64
Wk 30	<50

Colson. CROI 2024. Abstr 208.

Slide credit: clinicaloptions.com

ARTISTRY 1 ‡

BIC/LEN in Virologically Suppressed PLWH on Stable Complex ART Regimens

N = 671

Operationally seamless, randomized, open-label, multicentered study

Outcomes (by FDA Snapshot): Proportion of participants With HIV-1 RNA ≥ 50 copies/mL at Week 24 (Phase 2) and Week 48 (Phase 3)

August 2022 – ongoing

Study Sites: United States, Australia, Canada, Dominican Republic, France, Germany, South Korea, South Africa, Argentina, Japan, Italy, Spain, Taiwan, Thailand, United Kingdom & Puerto Rico

Adults VS for 6 months

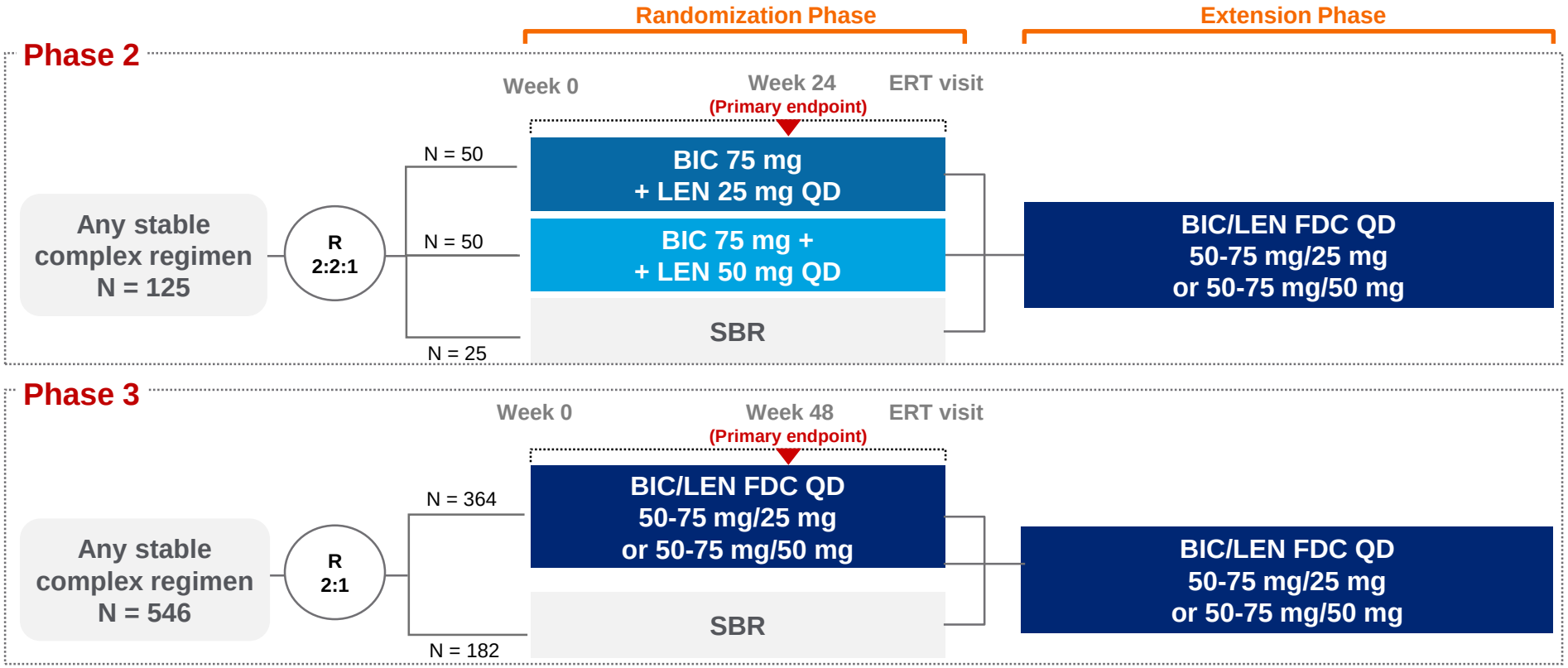
VL ≤ 50 copies/ml

On a complex ART regimen

No history of exposure to LEN or resistance to INSTIs

No history of HBV infection

eGFR ≥15 mL/min, not on HD/PD



ART, antiretroviral therapy; ERT, end of randomized treatment; FDC, fixed dose combination; HD, hemodialysis; PD, peritoneal dialysis; SBR, stable baseline regimen; STR, single tablet regimen; VL, viral load; VS, virologically suppressed

1. Clinicaltrials.gov NCT05502341 https://clinicaltrials.gov/ct2/show/NCT05502341?term=BIC%2FLEN&draw=2&rank=1 Accessed August 2022. 2. Gilead Sciences. Data on File

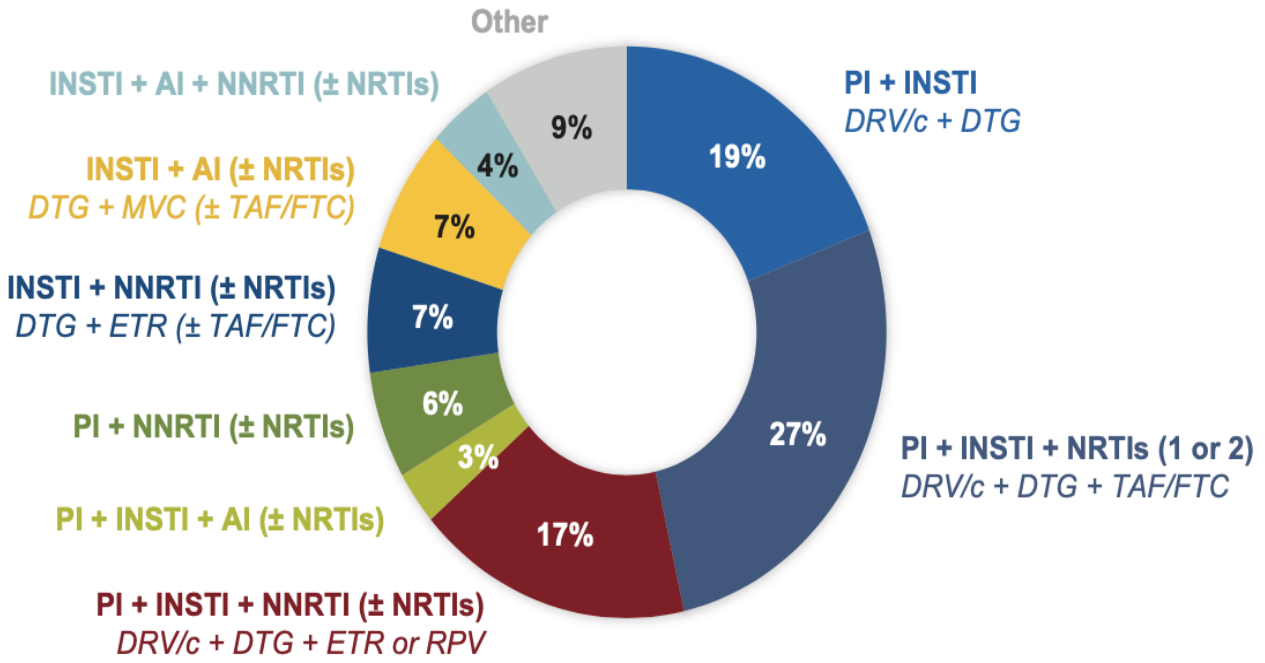
Phase 2 Study of Switch to Daily BIC + LEN in Individuals on a Complex HIV Treatment Regimen

Demographic and Baseline Characteristics

	BIC 75 mg + LEN 25 mg N = 51	BIC 75 mg + LEN 50 mg N = 52	SBR N = 25	Total N = 128
Age, years, median (range)	62 (26, 79)	62 (34, 76)	58 (41, 70)	60 (26, 79)
Female at birth, n (%)	13 (25.5)	7 (13.5)	4 (16.0)	24 (18.8)
Race, n (%) Asian White Black Other	 2 (3.9) 29 (56.9) 18 (35.3) 2 (3.9)	 2 (3.8) 34 (65.4) 16 (30.8) 0	 0 20 (80.0) 5 (20.0) 0	 4 (3.1) 83 (64.8) 39 (30.5) 2 (1.6)
Ethnicity,[a] n (%) Hispanic or Latinx Not Hispanic or Latinx	 7 (14.0) 43 (86.0)	 9 (17.6) 42 (82.4)	 4 (16.0) 21 (84.0)	 20 (15.9) 106 (84.1)
HIV-1 RNA ≥ 50 c/mL,[b] n (%)	0	2 (3.8)	0	2 (1.6)
CD4 count, cells/μL, median (Q1, Q3)	583 (460, 764)	624 (517, 791)	585 (285, 733)	610 (435, 766)
CD4 count < 200 cells/μL, n (%)	1 (2.0)	1 (1.9)	2 (8.0)	4 (3.1)
Past medical history of AIDS, n (%)	14 (27.5)	10 (19.2)	2 (8.0)	26 (20.3)
Duration of HIV treatment, years,[c,d] median (Q1, Q3)	27.8 (22.7, 32.4)	27.0 (18.9, 31.5)	26.9 (19.8, 31.9)	27.0 (19.9, 32.0)
Number of prior ARTs, median (Q1, Q3)	4.0 (2.0, 9.0)	7.0 (3.0, 11.0)	8.0 (3.0, 13.0)	6.0 (3.0, 11.0)
Historical resistance mutations,[e] n (%) INSTI NNRTI NRTI PI	 0 25 (49.0) 31 (60.8) 18 (35.3)	 0 28 (53.8) 35 (67.3) 17 (32.7)	 0 14 (56.0) 16 (64.0) 11 (44.0)	 0 67 (52.3) 82 (64.1) 46 (35.9)
Reasons for taking a complex regimen, n (%) History of resistance Intolerance to components of STRs Contraindication to STRs	 44 (86.3) 20 (39.2) 7 (13.7)	 40 (76.9) 11 (21.2) 4 (7.7)	 20 (80.0) 7 (28.0) 1 (4.0)	 104 (81.3) 38 (29.7) 12 (9.4)
Comorbidities, n (%) Dyslipidemia Diabetes mellitus Hypertension Chronic kidney disease	 39 (76.5) 36 (70.6) 34 (66.7) 12 (23.5)	 37 (71.2) 36 (69.2) 29 (55.8) 13 (25.0)	 20 (80.0) 16 (64.0) 15 (60.0) 4 (16.0)	 96 (75.0) 88 (68.8) 78 (60.9) 29 (22.7)

Phase 2 Study of Switch to Daily BIC + LEN in Individuals on a Complex HIV Treatment Regimen

Diversity of Complex ART Regimens in Phase 2



N = 128. The most common regimen(s) are shown in italics in each regimen category box; this is not an exhaustive list. Percentages do not sum to 100% due to rounding.
AI, attachment inhibitor; DRV/c, darunavir/cobicistat; DTG, dolutegravir; ETR, etravirine; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; MVC, maraviroc; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitor; PI, protease inhibitor; RPV, rilpivirine; TAF, tenofovir alafenamide.

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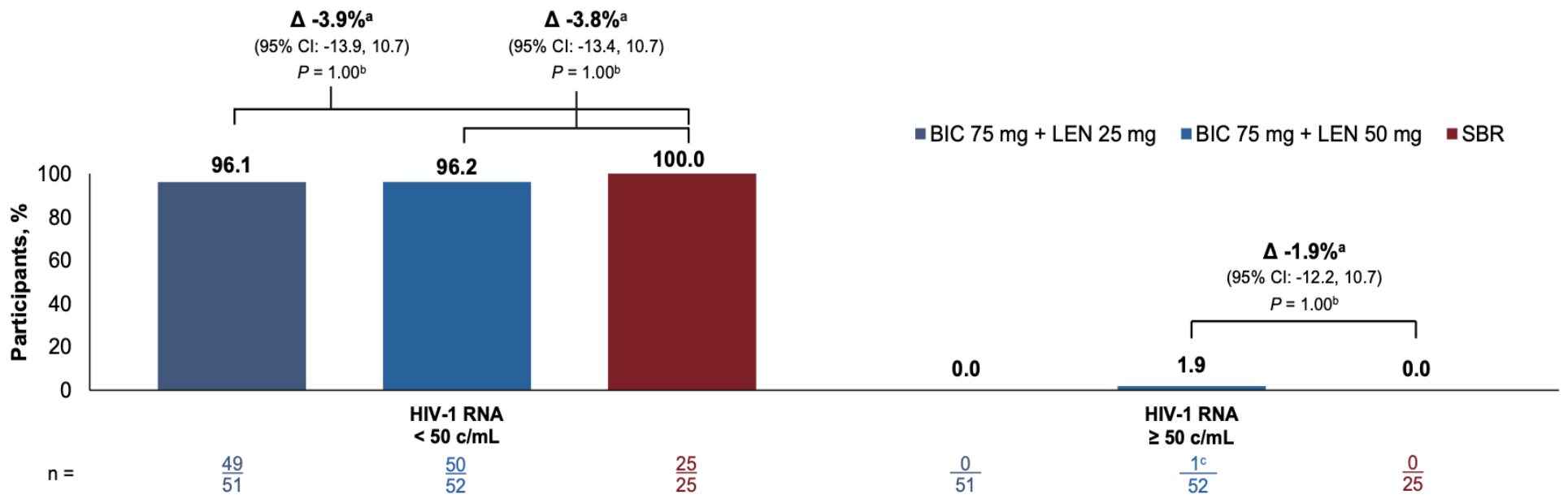
Virologic Outcome at Week 24 (FDA Snapshot Algorithm)



Two participants (3.9%) in the BIC 75 mg + LEN 25 mg group and one (1.9%) in the BIC 75 mg + LEN 50 mg group had no virologic data in the Week 24 window; reasons: one participant (2.0%) in the BIC 75 mg + LEN 25 mg group and one (1.9%) in the BIC 75 mg + LEN 50 mg group discontinued study drug due to an AE/death and last available HIV-1 RNA < 50 c/mL, and one participant (2.0%) in the BIC 75 mg + LEN 25 mg group discontinued study drug due to other reasons and last available HIV-1 RNA < 50 c/mL.

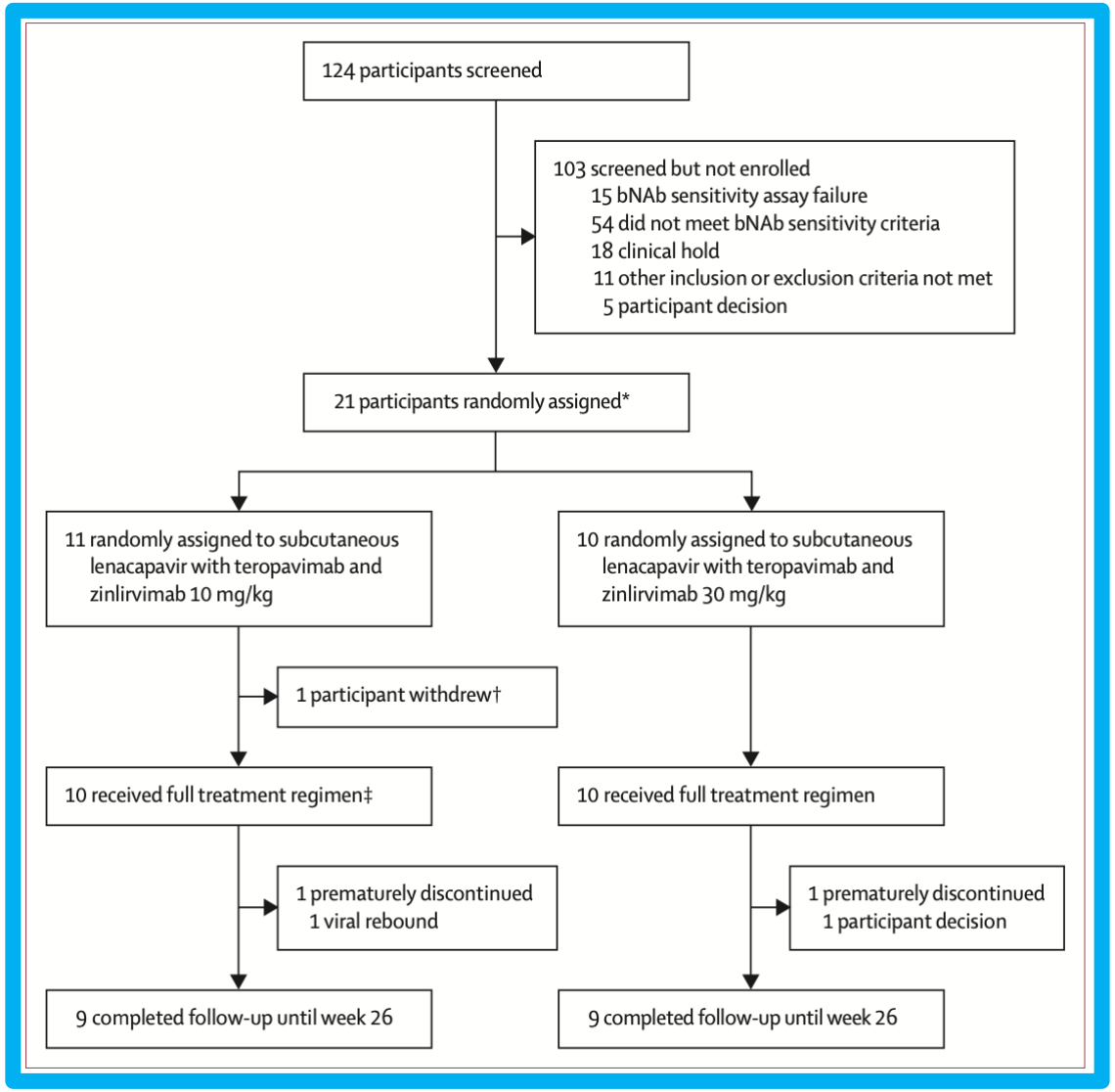
[a]Difference in % (95% CI): BIC + LEN – SBR calculated based on an unconditional exact method using two inverted one-sided tests.

[b]Based on Fisher exact test.

[c]HIV-1 RNA ≥ 50 c/mL in Week 24 window (later suppressed to < 50 c/mL without regimen change). No genotype/phenotype was performed as virologic failure did not reach threshold as per protocol (> 200 c/mL).

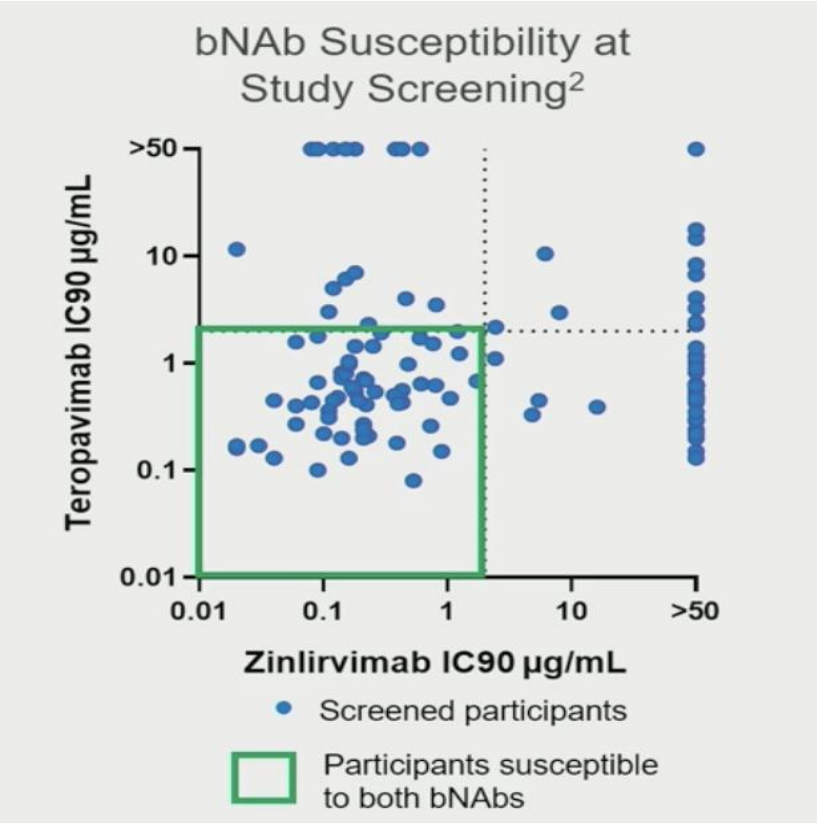
AE, adverse event; BIC, bictegravir; c, copies; FDA, Food and Drug Administration; LEN, lenacapavir; SBR, stable baseline regimen.

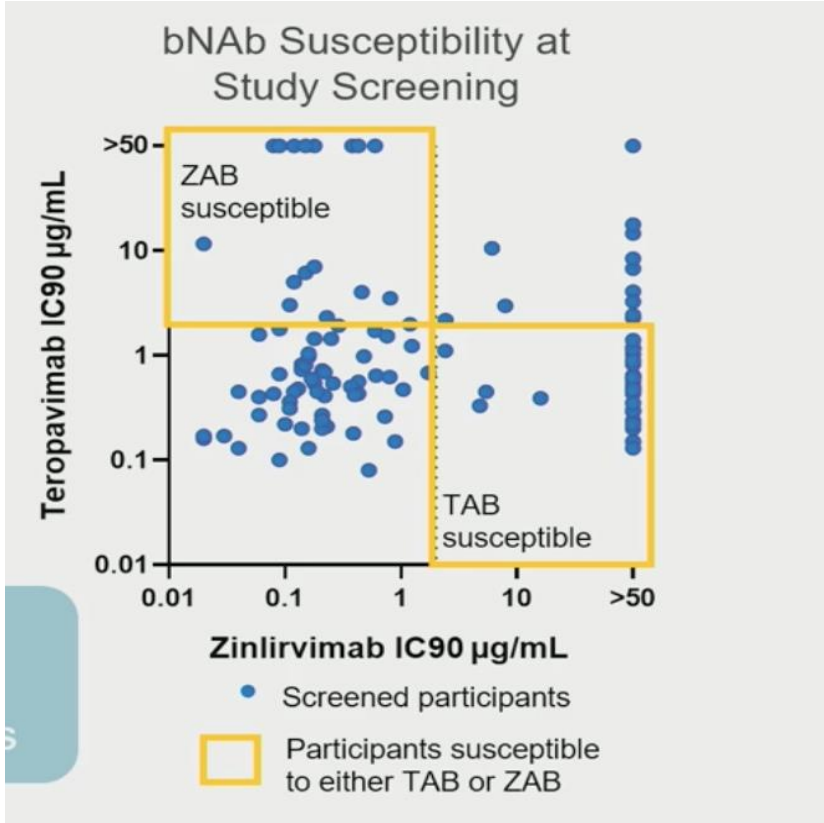
Teropavimab and zinlirvimab with lenacapavir once every 6 months for HIV treatment : trial profile



Eron JJ Lancet HIV 2024

Figure 4. Teropavimab (TAB) and zinlirvimab (ZAB) susceptibility at screening in the LEN+TAB+ZAB Phase 1 Studies





18 out of 20 participants susceptible to both bNAbs mantained 26 weeks virological suppression*

* Eron JJ, Lancet HIV 2024

8 out of 10 participants susceptible to either TAB or ZAB mantained 26 weeks virological suppression**

** Eron JJ, CROI 2024

TEROPAVIMAB AND ZINLIRVIMAB SENSITIVITY IN PEOPLE LIVING WITH MDR HIV-1: PRESTIGIO REGISTRY DATA

Vincenzo Spagnuolo[1], Laura Galli[1], Aiyappa Parvangada[2], Keith Dunn[2], Filippo Lagi[3], Roberta Gagliardini[4], Loredana Sarmati[5], Anna Maria Cattelan[6], Andrea Giacomelli[7], Maria Mercedes Santoro[8], Maurizio Zazzi [9], Christian Callebaut[2], Antonella Castagna[1], Laurie A. VanderVeen[2]

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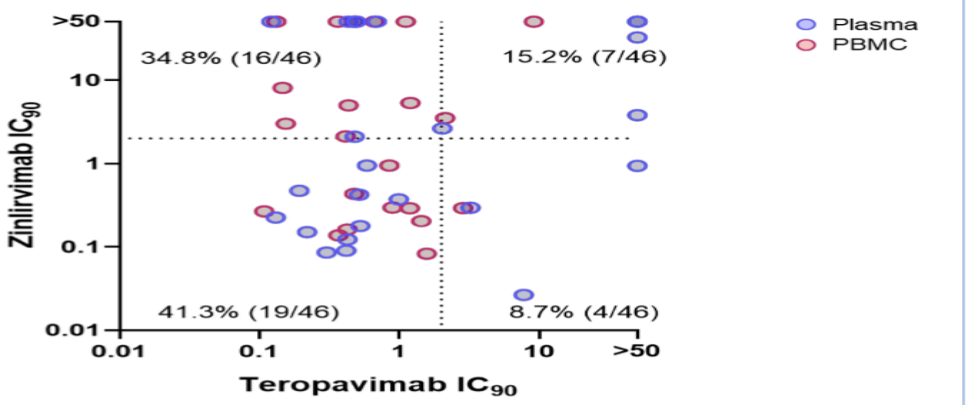
691

Figure 1: Distribution of TAB and ZAB IC_{90} values among PWH included in the study



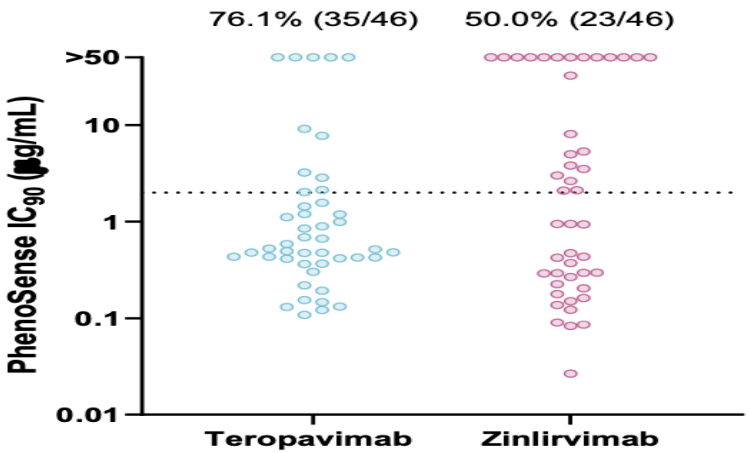
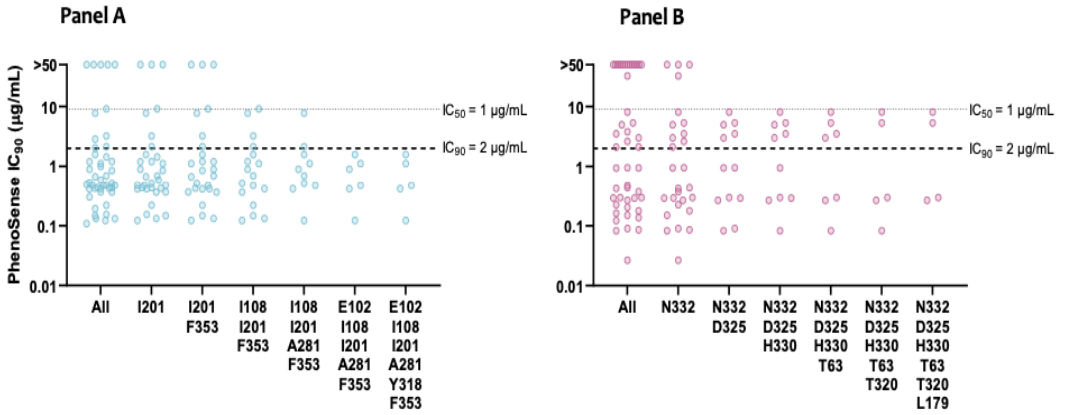
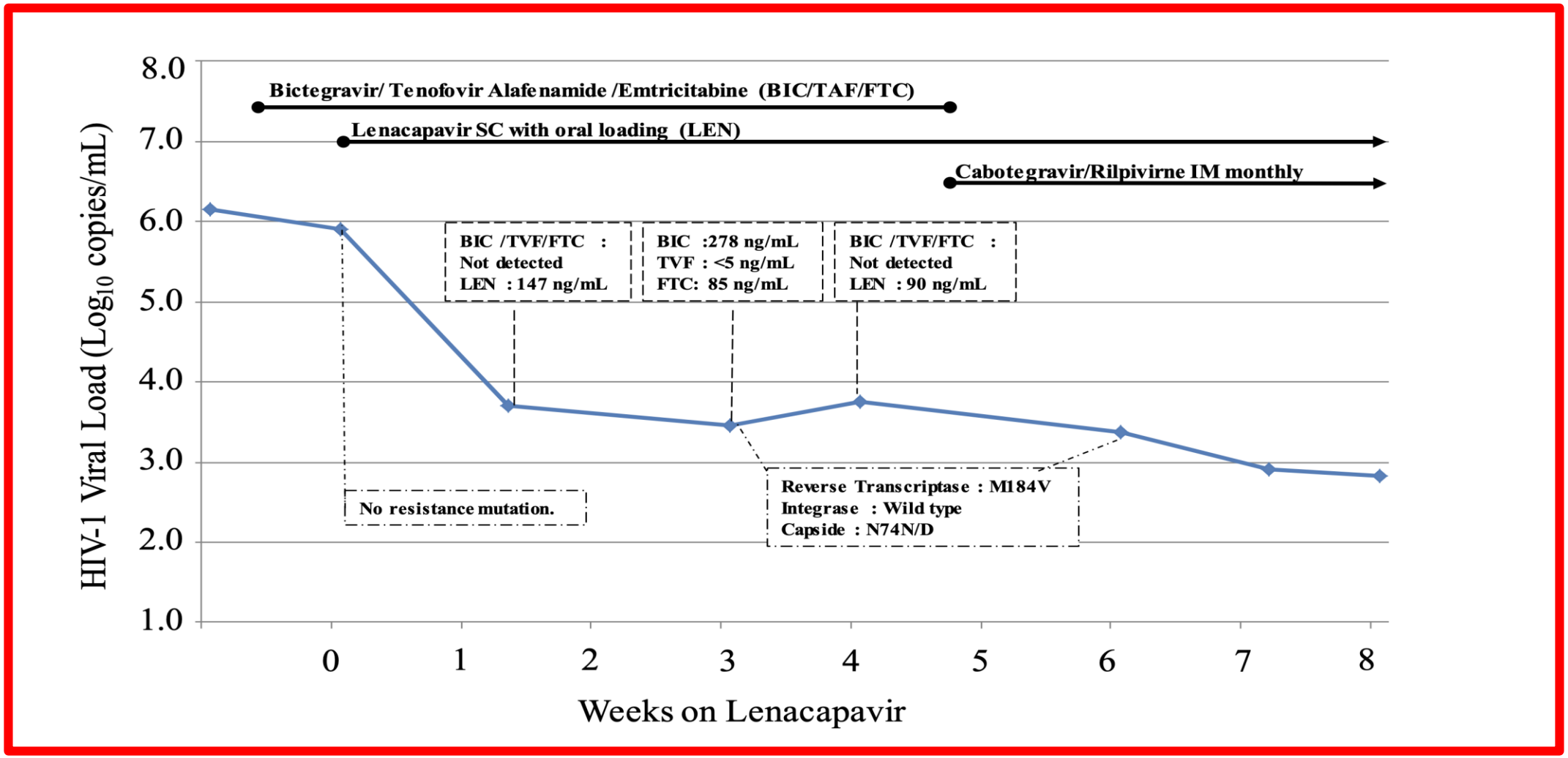


Figure 2: Prediction of Phenotypic Susceptibility by Genotypic Signatures



RNA viruses and DNA proviruses from individual participants were plotted based on presence of HIV-1 envelope signatures for TAB (Panel A) and ZAB (Panel B) sensitivity. "All" indicates all participants independent of presence of HIV-1 envelope signatures. Dashed line represents IC90 value = 2 µg/mL. Dotted line indicating IC50 = 1 µg/mL included for comparison to other studies[4]

Ultra-rapid selection of the N74D capsid inhibitor resistance mutation after 3 weeks on lenacapavir



M. Wirden, JAC 2024

Case Series of People With HIV on the Long-Acting Combination of Lenacapavir and Cabotegravir: Call for a Trial

Monica Gandhi,[1] Lucas Hill,[2] Janet Grochowski,[1] Alexander Nelson,[3] Catherine A. Koss,[1] Francis Mayorga-Munoz,[1] Jon Oskarsson,[1] Mary Shiels,[1] Ann Avery,[4] Laura Bamford,[2] Jillian Baron,[5] William R. Short,[5] and Corrilynn O. Hileman[4]

[1]Division of HIV, Infectious Diseases and Global Medicine, University of California, San Francisco (UCSF), San Francisco, California, USA, [2]Division of Infectious Diseases and Global Public Health, University of California San Diego (UCSD), San Diego, California, USA, [3]Department of Specialty Pharmacy, MetroHealth Medical Center, Cleveland, Ohio, USA, [4]Division of Infectious Diseases, MetroHealth Medical Center, and Case Western Reserve University (CWRU), Cleveland, Ohio, USA, and [5]Division of Infectious Diseases, Hospital of the University of Pennsylvania (UPenn), Philadelphia, Pennsylvania, USA

Background. Injectable cabotegravir (CAB)/rilpivirine (RPV) is the only combination long-acting (LA) antiretroviral regimen approved for HIV. RPV may not be effective among individuals with non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance, which has >10% prevalence in many countries. Lenacapavir (LEN) is an LA capsid inhibitor given every 6 months, but has not been studied in combination with other LA agents.

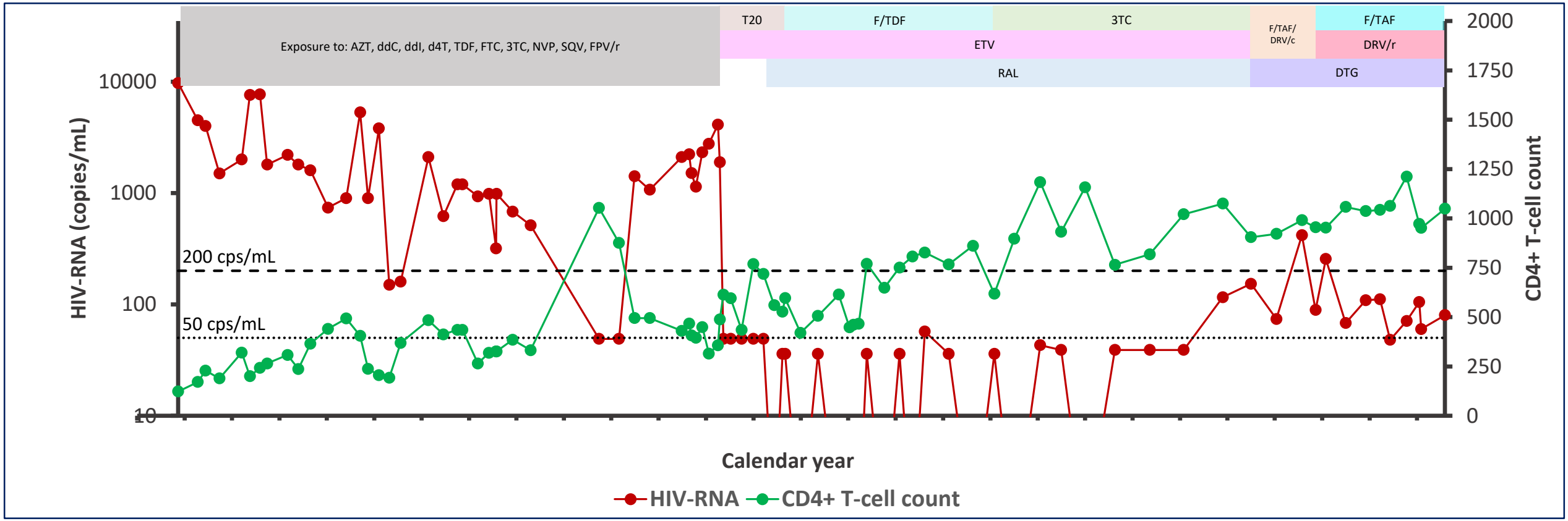
Methods. We assembled a case series from 4 US academic medical centers where patients with adherence challenges were prescribed LEN subcutaneously every 26 weeks/CAB (+/− RPV) intramuscularly every 4 or 8 weeks. Descriptive statistics, including viral load (VL) outcomes, were summarized.

Results. All patients (n = 34: 76% male; 24% cis/trans female; 41% Black; 38% Latino/a; median age [range], 47 [28–75] years; 29% and 71% on CAB every 4 or 8 weeks) reported challenges adhering to oral ART. The reasons for using LEN/CAB with or without RPV were documented or suspected NNRTI mutations (n = 21, 59%), integrase mutations (n = 5, 15%), high VL (n = 6, 18%), or continued viremia on CAB/RPV alone (n = 4, 12%). Injection site reactions on LA LEN were reported in 44% (32% grade I, 12% grade 2). All patients but 2 (32/34; 94%) were suppressed (VL <75 copies/mL) after starting LEN at a median (range) of 8 (4–16) weeks, with 16/34 (47%) suppressed at baseline.

Conclusions. In this case series of 34 patients on LEN/CAB, high rates of virologic suppression (94%) were observed. Reasons for using LEN/CAB included adherence challenges and underlying resistance, mostly to NNRTIs. These data support a clinical trial of LEN/CAB among persons with NNRTI resistance.

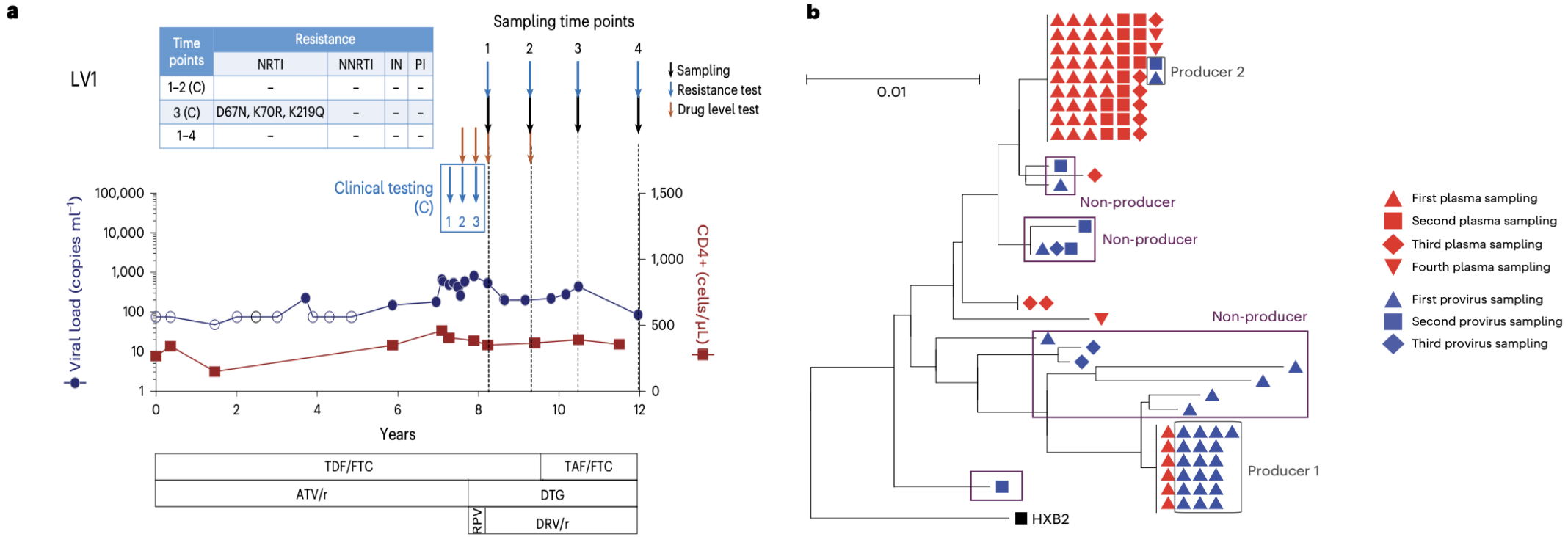
GS, M 64

- HIV since 1990 (stage C3 CDC-classification; CD4+ nadir: 79 cell/mm3 in 1990), on ART since 1991, on cART since 1996
- HCV coinfection (1999) → Liver cirrhosis (2008) → HCC (2021)



Courtesy of Clemente T

Viral and host mediators of non-suppressible HIV-1 viremia



A. Mohammadi, Nat med 2023

DRUGS	HG GRT	NGS GRT 2023
NRTI	**M41L, D67N, L74V, M184V, L210W, T215Y, K219R**	**M41L, D67N, L75I, M184V L210W, T215Y,**
3TC		
ABC		
FTC		
AZT		
TDF		
NNRTI	**K101E, Y181C, G190A**	**NONE**
DOR		
EFV		
ETR		
NVP		
RPV		
PI	**G48V, I50V, I54V, V82A, L90M**	**L10I, M46L, G48V, I54V, L63P, A71V, V77I, V82A, L90M, I93L**
ATV/r		
DRV/r		
LPV/r		
FPV/r IDV/r NFV SQV/r		
TPV/r		
INSTI	**Not Available**	**74I, 232N, 138A**
RAL		
EVG		
DTG		
BIC		
CAB		

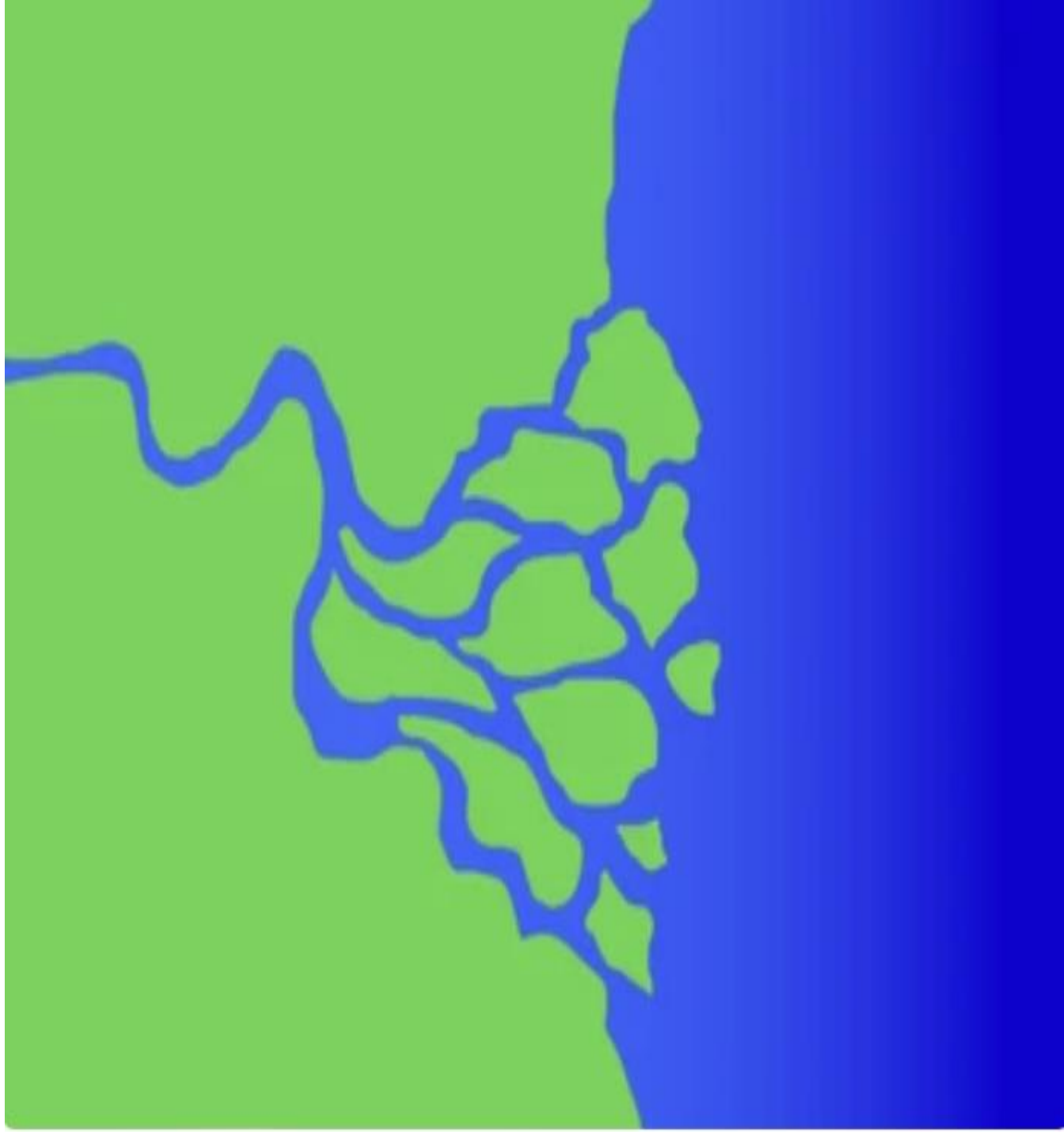
Male, 69 yo

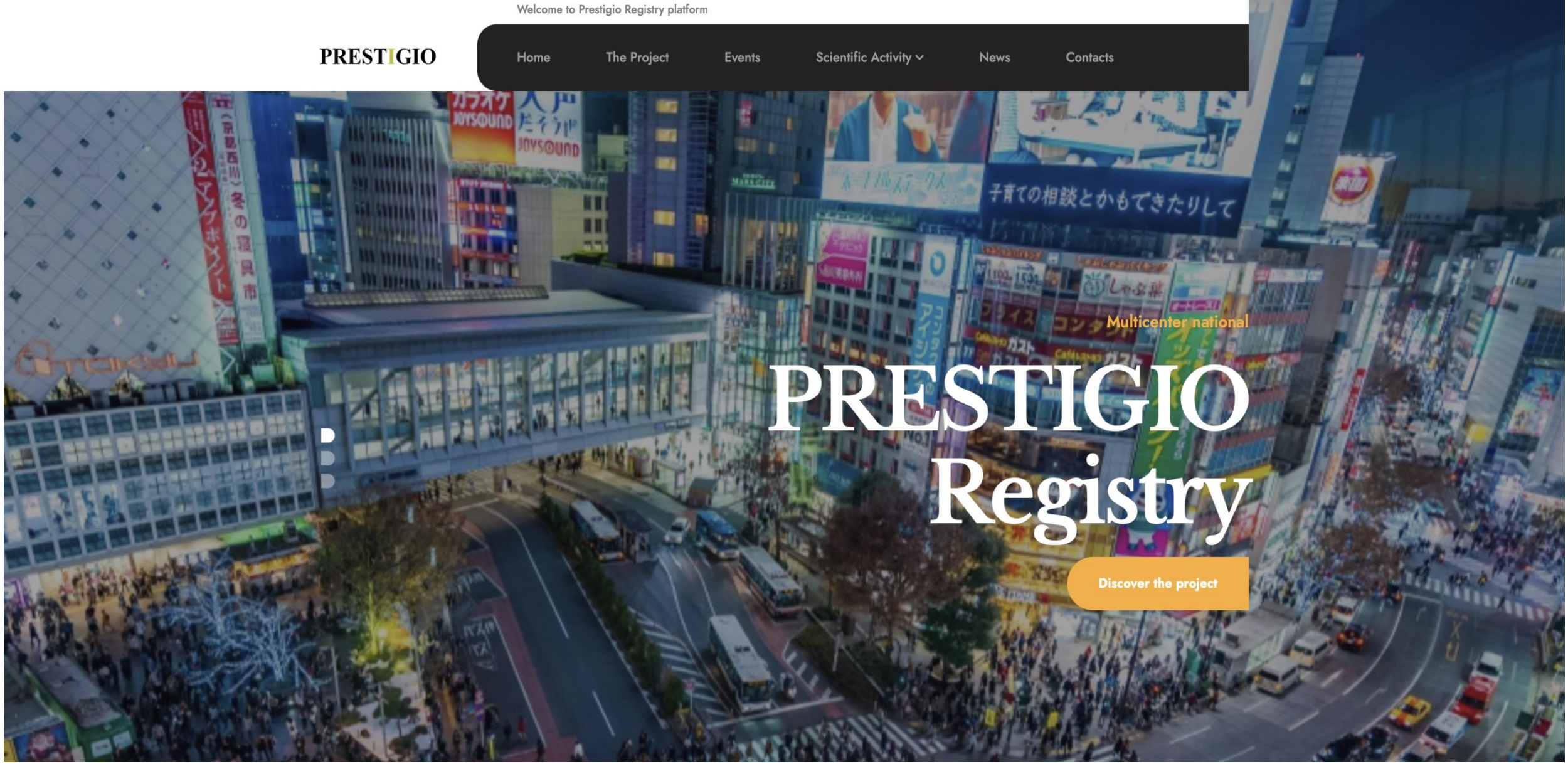
DTG BID + DRV/r 600/100 BID + FTR

204 cp/ml (11/2022)
27 cp/ml (01/2023)
107 cp/ml (04/2023)
137 cp/ml (09/2023)

Courtesy of L. Comi

Manage new options to maintain long-term undetectability avoid further resistance and improve quality of life





website

https://registroprestigio.org